1: *J Endocrinol* 1999 Sep;162(3):371-9 Related Articles, Books, LinkOut

JOE Online

Effects of dexamethasone on proliferation, activity, and cytokine secretion of normal human bone marrow stromal cells: possible mechanisms of glucocorticoid-induced bone loss.

Kim CH, Cheng SL, Kim GS

Division of Endocrinology, Department of Internal Medicine, Soonchunhyang University College of Medicine, Seoul, Korea.

It is well documented that glucocorticoid excess causes bone loss, but the mechanisms of these effects remain poorly defined. To understand further the mechanisms of glucocorticoid-induced osteoporosis, we investigated the effects of glucocorticoids on bone formation and bone resorption by examining the proliferation, functional activities, and cytokine secretion of cultured human bone marrow stromal cells (hBMSC). Treatment with dexamethasone for 24 h at the concentration of 10(-8) M significantly suppressed [(3)H]thymidine incorporation and further inhibition was observed with longer treatment (8 days) or higher concentration (10(-7) M). Alkaline phosphatase activity of hBMSC was markedly stimulated with addition of dexamethasone (10(-8) M), to 191 +/- 22% (after 4 days) and 317 +/- 46% (after 7 days) of control. Dexamethasone (10(-8) M) treatment for 48 h decreased the incorporation of [(3)H]proline into collagenase-digestible protein (CDP; 43.7+/-7.9% of control) and non-collagen protein (65.2+/-8.4% of control), with a greater effect on CDP. Northern blot analysis indicated that alpha1(I)-collagen mRNA level was decreased by dexamethasone to 27.6 +/- 9.0% of the control value after 1 day of exposure, and to 55.2 +/- 6.2% after 7 days. Dexamethasone markedly suppressed basal production of interleukin (IL)-6 and IL-11 and that stimulated by parathyroid hormone (PTH), IL-1alpha, or tumour necrosis factor-alpha in a dose-dependent manner. These results suggest that the glucocorticoid-induced bone loss is derived at least in part via inhibition of bone formation, which includes the suppression of osteoblast proliferation and collagen synthesis. As both basal and PTH-stimulated production of IL-6 and IL-11 are decreased by dexamethasone, the increased bone resorption observed in glucocorticoid-induced osteopenia does not appear to be mediated by IL-6 or IL-11.

PMID: 10467228, UI: 99398450